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10/622,675	07/17/2003	Paul F. Predki	0618.019.0002	3642

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INVITROGEN C/O INTELLEVATES
Sughrue Mion PLLC
P.O. BOX 52050
MINNEAPOLIS, MN 55402

EXAMINER	
AGRAWAL, RITESH	
ART UNIT	**PAPER NUMBER**
1631	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/29/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/622,675	PREDKI ET AL.	
	Examiner	Art Unit	
	Ritesh Agrawal	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 November 2006 and 01 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *2,3,6,11-14 and 19-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,5,7-10 and 15-18* is/are rejected.

7)☒ Claim(s) *1,4,5,7-10 and 15-18* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 July 2003 and 01 December 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Amendments

1. With respect to the original restriction requirement mailed 12/12/05:

Applicant's election with traverse of Group I (claims 1, 4-10, and 15-20) in the reply filed on 06/12/06 is acknowledged. The traversal is on the ground(s) that the Office had not established the inventions to be independent or distinct and that the Office had not established a search burden. This is not found persuasive because of the arguments made in the Office action mailed 09/12/06.

The requirement is still deemed proper and is therefore made FINAL.

Furthermore, with respect to the secondary requirement for an election of species mailed 09/12/06:

Applicant's election of degree of sequence homology reflects degree of sequence identity (claim 5), the region of the target protein is identified as containing the binding site (claim 15), and the region of the cross-reactive protein is identified as containing the binding site (claim 16) in the reply filed on 11/13/06 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 2-3, 6, 11-14, and 19-23 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention and species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 06/12/06.

Applicant's preliminary amendments filed 04/08/04, 06/12/06, and 12/01/06 are acknowledged and entered.

Specification

2. The disclosure is objected to because of the following:

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

Whereas the elected invention is drawn to methods for the prediction of any binding site, the title is specifically drawn to the prediction of an epitope.

Applicant is reminded of the proper content of an abstract of the disclosure.

A patent abstract is a concise statement of the technical disclosure of the patent and should include that which is new in the art to which the invention pertains. If the patent is of a basic nature, the entire technical disclosure may be new in the art, and the abstract should be directed to the entire disclosure. If the patent is in the nature of an improvement in an old apparatus, process, product, or composition, the abstract should include the technical disclosure of the improvement. In certain patents, particularly those for compounds and compositions, wherein the process for making and/or the use thereof are not obvious, the abstract should set forth a process for making and/or use thereof. If the new technical disclosure involves modifications or alternatives, the abstract should mention by way of example the preferred modification or alternative.

The abstract should not refer to purported merits or speculative applications of the invention and should not compare the invention with the prior art.

Where applicable, the abstract should include the following:
(1) if a machine or apparatus, its organization and operation;
(2) if an article, its method of making;
(3) if a chemical compound, its identity and use;
(4) if a mixture, its ingredients;
(5) if a process, the steps.

Extensive mechanical and design details of apparatus should not be given.

The abstract of the disclosure is objected to because the abstract is specifically drawn to methods for the determination of an epitope, whereas the elected invention is drawn to methods for the prediction of any binding site. Correction is required. See MPEP § 608.01(b).

Appropriate correction is required.

Claim Rejections - 35 USC § 101

3. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1, 4-5, 7-10, and 15-18 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The following analysis of facts of this particular patent application follows the analysis suggested in the "Interim Guidelines for Examination of Patent Applications for Patent Subject Matter Eligibility"[1]. Note that the text of the Guidelines is italicized.

To satisfy section 101 requirements, the claim must be for a practical application of the § 101 judicial exception, which can be identified in various ways (Guidelines, p. 19):

- The claimed invention "transforms" an article or physical object to a different state or thing.

- The claimed invention otherwise produces a useful, concrete and tangible result, based on the factors discussed below.

[1] Available at http://www.uspto.gov/web/offices/pac/dapp/opla/preognotice/guidelines101_20051026.pdf

In the instant case, the claimed invention does not "transform" an article or physical object to a different state or thing because it merely carries out sequence comparisons. This does not preclude the subject matter to be patentable as, for eligibility analysis, as

> *physical transformation "is not an invariable requirement, but merely one example of how a mathematical algorithm [or law of nature] may bring about a useful application." AT&T, 172 F.3d at 1358-59, 50 USPQ2d at 1452. If the examiner determines that the claim does not entail the transformation of an article, then the examiner shall review the claim to determine if the claim provides a practical application that produces a useful, tangible and concrete result. In determining whether the claim is for a "practical application," the focus is not on whether the steps taken to achieve a particular result are useful, tangible and concrete, but rather that the final result achieved by the claimed invention is "useful, tangible and concrete." The claim must be examined to see if it includes anything more than a § 101 judicial exception. If the claim is directed to a practical application of the § 101 judicial exception producing a result tied to the physical world that does not preempt the judicial exception, then the claim meets the statutory requirement of 35 U.S.C. § 101. If the examiner does not find such a practical application, the examiner has determined that the claim is nonstatutory. (Guidelines, p. 20)*

The question is thus whether the final result achieved by the claimed invention satisfies all three criteria of being useful, and concrete, and tangible.

Furthermore, the useful, tangible, and concrete result must be recited in the claim itself, rather than addressed in specification.

(2) **"TANGIBLE RESULT"** The tangible requirement does not necessarily mean that a claim must either be tied to a particular machine or apparatus or must operate to change articles or materials to a different state or thing. However, the tangible requirement does require that the claim must recite more than a § 101 judicial exception, in that the process claim must set forth a practical application of that § 101 judicial exception to produce a real-world result. The opposite meaning of "tangible" is "abstract."

The instant claims are drawn to computational means for comparing sequences. However, as claimed, at least one embodiment of the method does not produce a

tangible result. For example, the method as claimed may take place entirely within the confines of a computer or a human mind without any communication to the outside world and without using or making available for use, the results of the computation. Thus, the instant methods of the claims do not produce any tangible result.

Therefore, the final result achieved by the claimed invention does not satisfy all three criteria of being useful, and concrete, and tangible.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1, 4-5, 7-10, and 15-18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for predicting at least part of a binding site for a molecule in a target protein when the target protein is known to be cross-reactive for the molecule with other proteins, does not reasonably provide enablement for predicting a binding site for any target protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. This rejection is applied in light of the breadth of the claim limitations.

The analysis is carried out with respect to the Wands factors of (a) the quantity of experimentation; (b) the amount of guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the

predictability of the prior art; (g) the breadth of the claims; and (h) the relative skill in the art:

(a) The amount of experimentation required by the skilled artisan in order to practice the process of the claim would be unpredictable because:

(b) The applicant provides little guidance as to how to predict a binding site in any putative target protein based upon sequence comparison with other proteins putatively bound by a molecule.

(c) The instant application provides a working example for the prediction of a binding site for an antibody to HDA1 in the HDA1 sequence when the HDA1 amino acid sequence is compared with the sequence of other proteins who have empirically been shown to be cross-reactive with the antibody to HDA1.

(d)-(f) The nature of the invention is some computational means by which to predict binding sites in target proteins based upon sequence comparisons to other proteins. Applicant's own specification specifically states that, "although sequence analysis is useful in explaining the observed cross-reactivity, it is clearly insufficient to predict it" (page 56, lines 23-24). Hence applicant's own specification clearly states that applicant's method can only be used to predict binding sites for a molecule in a target protein when the protein is already known to be bound by the molecule.

(g)-(h) The claims are broad and encompass the prediction of a molecule's binding site in any protein that *can* be bound by the molecule. Since applicant does not specifically limit proteins that "can be bound by a molecule" applicant's claim presently covers the prediction of binding sites in essentially any protein since almost any protein

could potentially bind any molecule with some degree of affinity regardless of whether the protein is truly cross-reactive for that molecule. While the relative skill in the art is high, the methodology required by the claims of the current invention are complex and not well known.

The skilled practitioner would first turn to the instant specification for guidance on how to predict a molecule's binding site in a target protein using sequence analysis regardless of whether or not the protein is actually cross-reactive for the molecule. However, the specification does not provide sufficient guidance for carrying out such analysis and even suggests that "empirical assessment of cross-reactivity . . . [is] necessary" (page 51, lines 17-18). As a result, the practitioner would then turn to the art for those methodologies but the art concurs with the unpredictability of the methods (Michaud et al., Nature Biotechnology, 2003, vol. 21, pages 1509-1512), see in particular, page 1510, 2nd column, 1st paragraph. As a result, the practitioner would have to turn to their own experimentation to develop methodologies which the art suggest are difficult problems. Therefore the skilled practitioner would be subject to the burden of undue experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1, 4-5, 7-10, and 15-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the phrase," comparing, for each of a plurality of cross-reactive proteins" in line 4. It is unclear whether these proteins are cross-reactive amongst themselves, are cross-reactive with the target protein, or both.

Claim 1 recites the phrase, "said cross-reactive protein" in line 6. Since the claim recites a plurality of cross-reactive proteins, it is unclear to which of these proteins the phrase refers.

Claim 1 recites the limitation "the sequence homologies" in line 11. There is insufficient antecedent basis for this limitation in the claim. There is no prior reference to a "sequence homology."

Claim 5 recites the limitation "the degree of sequence homology" in line 1-2. There is insufficient antecedent basis for this limitation in the claim. There is no prior reference to a "degree of sequence homology" in claim 5, or claim 1, from which it depends.

Claim 8 recites the limitation "said plurality of amino acid sequences of each said cross-reactive protein" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim. There is no reference to a "plurality of amino acid sequences of each cross-reactive protein" in claim 8 or claim 1, from which it depends.

Claim 16 recites the limitation "the cross-reactive protein" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim. Claim 1, from which claim 16 depends, recites multiple cross-reactive proteins. It is unclear as to which of the proteins the phrase refers.

Claim 17 recites the limitation "the entire contiguous amino acid sequence of the target protein" in line 2. There is insufficient antecedent basis for this limitation in the claim. There is no prior reference to an entire contiguous amino acid sequence of a target protein in claim 17, or claim 1, from which it depends.

Claim 18 recites the limitation "the entire contiguous amino acid sequence of the cross-reactive protein" in lines 2-3. There is insufficient antecedent basis for this limitation in the claim. There is no prior reference to an entire contiguous amino acid sequence of a cross-reactive protein in claim 18, or claim 1, from which it depends.

Claim 18 recites the limitation "the cross-reactive protein" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim. Claim 1, from which claim 18 depends, recites a "plurality of cross-reactive proteins." It is therefore unclear as to which of these proteins the phrase refers.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claim 1, 4-5, and 15-18 rejected under 35 U.S.C. 102(b) as being anticipated by Aguas et al. (Infection and Immunity, Vol. 58, Pages 1461-1470, May 1990).

The claims are drawn to a method for predicting at least a part of a binding site in a target protein comprising:

a) comparing a plurality of amino acid sequences in a region of the target protein with each of a plurality of amino acid sequences from each of a plurality of cross-reactive proteins

b) identifying an amino acid sequence of the target protein having the greatest homology to the cross-reactive proteins as the binding site in the target protein

Aguas et al. disclose comparing amino acid sequences from the 65 kDa Mycobaterial Heat Shock protein with amino acid sequences from cross-reactive lactoferrin, transferrin, and Dr_{β} subsets of the MHC II complex molecules (abstract, lines 5-9). Through their comparison comparison, they identify the tetrapeptide KDLL as the binding site for the cross-reactive antibody because it has the greatest homology among the various proteins (page 1467, 1st column, 1st paragraph, lines 4-5 and 2nd column).

With respect to claim 4, Aguas et al. disclose that they are looking for an epitope bound by a common antibody (page 1461, 1st column, 1st paragraph).

With respect to claim 5, Aguas et al. are only looking for sequences that are identical between the compared amino acid sequences, therefore, the homology reflects sequence identity (for example, see table 1).

With respect to claims 15-18, Aguas et al. disclose are comparing regions consisting of the entire contiguous amino acid sequence (page 1465, 1st column, 3rd paragraph) as well as regions containing the binding site (page 1465, 2nd column, 1st paragraph). Furthermore, since the entire contiguous sequence of the 65 kDa Mycobaterial Heat Shock protein contains the binding site, the disclosure of comparison

of the entire sequence, represents a disclosure of a region identified as containing the binding site.

7. Claims 1, 4-5, 7-10, and 15-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Golding et al. (Journal of Experimental Medicine, Vol. 167, Pages 914-923, March 1988).

The claims are drawn to a method for predicting at least a part of a binding site in a target protein comprising:

a) comparing a plurality of amino acid sequences in a region of the target protein with each of a plurality of amino acid sequences from each of a plurality of cross-reactive proteins

b) identifying an amino acid sequence of the target protein having the greatest homology to the cross-reactive proteins as the binding site in the target protein

Golding et al. disclose comparing HLA class II sequences with HIV I protein sequences (page 916, 1st paragraph, lines 12-16) and identifying an amino acid sequence of the greatest homology in these cross-reactive proteins (page 916, 1st paragraph, lines 16-19).

With respect to claim 4, Golding et al. disclose that the identified sequence serves as an epitope that is cross-reactive for an antibody (page 916, 3rd paragraph).

With respect to claim 5, the degree of sequence homology reflects the degree of sequence identity (page 916, 1st paragraph, lines 17-18).

With respect to claims 7-10, Golding et al. disclose that their comparison of the amino acid sequences is carried out using the SFASTP sequence alignment program (page 915, 2nd paragraph, lines 3-7). One of ordinary skill in the art would recognize that in aligning a set of protein sequences, sequence alignment programs work by aligning successive overlapping subsequences in those sequences whereby the aligned sequences are offset by a single amino acid at each position in the generated alignment matrix. Furthermore, the algorithm upon which the SFASTP algorithm is based, specifically discloses sliding one sequence along the other to find aligned subsequences (see supporting document, Wilbur and Lipman, PNAS, vol. 80, pages 726-730, 1983; page 726, 2nd column, 3rd paragraph, lines 7-10).

With respect to claims 15-16, Golding et al. identify the compared regions as containing the binding site (see, as cited, for claim 4).

Claim Objections

8. Claims 1,4,5,7-10 and 15-18 are objected to because of the following informalities: Claim 1 recites steps a and b. Each step is followed by a period. A claim may only contain a single period. Appropriate correction is required.

Claims 7, and 9-10 are objected to because of the following informalities: Claim 7 recites the phrase "amino acid sequences comprises successive overlapping amino acid sequences". It appears that the term comprises should be in the singular form. Appropriate correction is required.

Claims 8, and 10 are objected to because of the following informalities: Claim 8 recites the phrase "plurality of amino acid sequences of each said cross-reactive protein comprises successive overlapping amino acid sequences". It appears that the term comprises should be in the singular form. Appropriate correction is required.

Claim 9 is objected to because of the following informalities: The claim recites the phrase "amino acid sequences pan said region of said target protein" in lines 1-2. It appears the term "pan" should be the term "span." Appropriate correction is required.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

9. Claims 1, 4-5, 7-10, and 15-18 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1, 4-5, 7-10, and 15-18 of copending Application No. 10/895226. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Conclusion

10. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ritesh Agrawal whose telephone number is (571) 272-2906. The examiner can normally be reached on 8:30 AM - 5:00 PM M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Ritesh Agrawal, PhD RA

SHUBO (JOE) ZHOU, PH.D.
PATENT EXAMINER